

cases. Jukes¹⁰ noted a like condition in rats on similar rations and suggested that a vitamin K deficiency might exist.

Conclusion. The effect of pantothenic acid in cure of nutritional achromotrichia is difficult to assess at present because other factors are clearly involved. Certain liver extracts providing as low as 40 μ g of pantothenic acid per day caused complete remission, while the effect of synthetic d-calcium pantothenate was negligible at best. The addition of d-calcium pantothenate to extracts low in this factor, however, increased their anti-graying potency. Age or weight increase of animals did not seem to influence the curative effect of supplements for graying.

Although rats were raised to maturity on highly synthetic diets supplying adequate d-calcium pantothenate, successful matings were not observed.

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Hyperplasia and Hypertrophy of the Mucosa of Larger Biliary Ducts in Mice Receiving Estrogens.*

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During the course of observations on mice which had received injections of various estrogens for prolonged periods an enlargement of the bile ducts was observed in many animals. In untreated mice the bile ducts, cystic duct, common duct and its branches, were small thread-like structures. Occasionally a slight cystic distension of the common bile duct was apparent at autopsy. The walls were delicate and when slightly distended almost transparent. Histologically the ducts had a thin and irregular muscularis, and a well-developed mucosa. The tall columnar epithelium was moderately folded on the loose underlying tissue of the lamina propria, and a few small glands extended to the serosa, especially in the common bile duct (Fig. 3).

The bile ducts of many mice which had received estrogens were grossly thickened to several times the size of the ducts of the untreated (Fig. 1). They are also rather rigid, white and somewhat

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nodular. Enlargement was usually greatest at the points of junction with the branches leading to the several lobes of the liver. The main duct tended to become smaller as it approached the gut. The cystic duct was usually thickened up to the neck of the gall bladder. The gall bladder was involved in only a few mice and in these it was reduced in size and histologically resembled the upper end of the cystic duct.

Microscopic examination of the enlarged ducts of the estrogen-

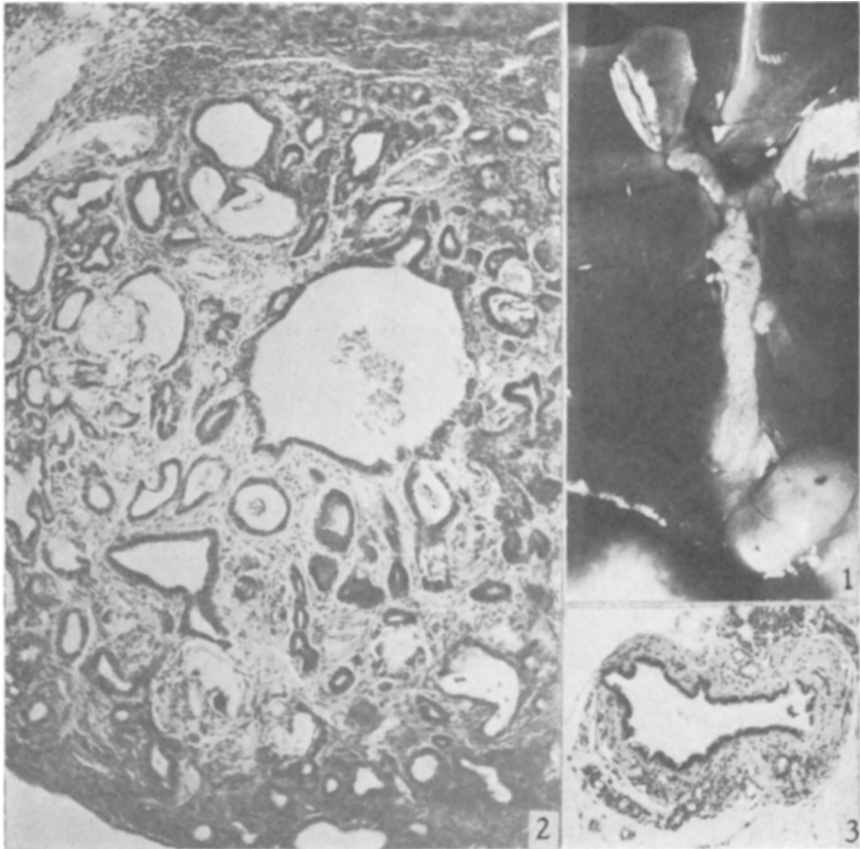


FIG. 1.

1. Gall bladder, cystic and common bile ducts of a F_1 hybrid mouse (A X C_3H) which had received 16.6 μg estradiol benzoate weekly for 247 days. The ducts are thickened and nodular.

2. A section through the common bile duct of a mouse of the C_3H strain, which had received 50 μg of estradiol benzoate weekly for 218 days. ($\times 90$.) The mucosa was thick and many gland-like processes extended to the serosa.

3. A section through the common bile duct of an untreated hybrid mouse (A X C_3H), killed at 273 days of age. $\times 90$.

treated mice uniformly showed an extensive increase of the epithelial folds and gland-like processes which completely penetrated the thickened mucosa, the muscularis and frequently projected to the serosa (Fig. 2). The epithelium consisted of tall columnar cells which showed slight mitotic activity. In many ducts 2 types of cells were found, tall cells with an eosinophilic cytoplasm and cells with a clear cytoplasm. Evidence of cystic distension of the ducts, concretions or inflammatory processes were seldom found and never extensive. The lamina propria was histologically unchanged and the muscularis showed no hypertrophy, in fact, was difficult to discern in many hypertrophied ducts. The larger branches of the common duct were similarly involved but the intrahepatic ducts had not been affected.

Hypertrophy of the biliary ducts was observed in many mice of several different inbred strains (CBA, C₅₇H, C₅₇, JK, A) and hybrids which have received estradiol dipropionate and estradiol benzoate in oily solution in amounts ranging from 16.6 to 50 μ g weekly, estrone pellets, or stilbestrol (250 μ g weekly). All animals were maintained on a diet of Purina Fox Chow and water. The hyperplasias occurred most frequently and were most extensive in mice receiving treatment for the longer periods. Most mice surviving treatment over 450 days showed lesions of the biliary ducts. In one series of experiments 58 of 76 mice (F₁ hybrids of CBA $\times$ C₅₇ strains) receiving 16.6 μ g of estradiol benzoate had moderately to extremely enlarged biliary ducts. Only 4 animals had ducts that were grossly normal. The incidence was lower in mice of groups which did tolerate the injections for the longer periods. Untreated mice (with the exception of 2 castrated females with adrenal tumors) and mice receiving testosterone propionate or sesame oil, have not shown a hypertrophy of the biliary ducts.

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Pulmonary Circulation Time in Man at Low Body Temperatures.

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Through the coöperation of Dr. Temple Fay, we have had an opportunity to observe a large number of patients during a period